

Claims

1. Nucleic acid which codes for the  $\alpha$  chain of a human T cell receptor, or for a functional derivative or a fragment thereof and which comprises a CDR3 region formed from a combination of a V $\alpha$ 20 and J $\alpha$ 22 gene segment.

2. Nucleic acid which codes for the  $\alpha$  chain of a human T cell receptor, or for a functional derivative or a fragment thereof and comprises a CDR3 region selected from:

(a) a nucleotide sequence coding for the amino acid sequence (SEQ ID NO: 23)

Y C L (X<sub>1</sub>...X<sub>n</sub>) S A R Q L T F (I)

in which X<sub>1</sub> ... X<sub>n</sub> represents a sequence of 3-5 amino acids,

(b) a nucleotide sequence which codes for an amino acid sequence which is at least 80 % identical with the amino acid sequence from (a), or

(c) a nucleotide sequence which codes for an amino acid sequence with an equivalent recognition specificity for the peptide component of the T cell receptor ligands.

*bio / dscp*

1  
2  
3  
4.

3. Nucleic acid as claimed in claim 2,  
wherein  
the amino acid sequence  $x_1 \dots x_n$  is selected from  
the group comprising the amino acid sequences VGG,  
VLSG, ATG, VSG, DSG, VVSG, ALAG, APSG and VGR.

5. Vector,  
wherein  
it contains at least one copy of a nucleic acid as  
claimed in one of the claims 1 to 4.

6. Cell,  
wherein  
it expresses a nucleic acid as claimed in one of  
the claims 1 to 4.

7. Cell,  
wherein  
it is transformed with a nucleic acid as claimed in  
one of the claims 1 to 4 or with a vector as  
claimed in claim 5.

8. Polypeptide,  
wherein  
it is coded by a nucleic acid as claimed in one of  
the claims 1 to 4.

II 9. Polypeptide as claimed in claim 8,  
wherein  
it comprises the variable domain of the  $\alpha$  chain of  
a human T cell receptor.

III 10. Nucleic acid which codes for the  $\beta$  chain of a human  
T cell receptor, or for a functional derivative or  
a fragment thereof and comprises a CDR3 region  
formed from a combination of a  $V\beta 22$  gene segment, a  
 $D\beta 1$  or  $D\beta 2$  gene segment and a  $J\beta$  gene segment in  
particular a  $J\beta 2.1$ ,  $J\beta 2.3$  or  $J\beta 2.7$  gene segment.

11. Nucleic acid which codes for the  $\beta$  chain of a human  
T cell receptor, or for a functional derivative or  
a fragment thereof and comprises a CDR3 region  
which is selected from:

(a) a nucleotide sequence coding for the amino acid  
sequence (SEQ ID NO: 24) and (SEQ ID NO: 45)  
respectively  
C A (X'<sub>1</sub> ... X'<sub>n</sub>) Y/D E Q Y F (II)

in which X'<sub>1</sub> ... X'<sub>n</sub> represents a sequence of  
5-7 amino acids,

(b) a nucleotide sequence coding for the amino acid  
sequence (SEQ ID NO: 25)

C A (X''<sub>1</sub> ... X''<sub>n</sub>) N E Q F F (III)

in which X''<sub>1</sub> ... X''<sub>n</sub> represents a sequence of  
5-7 amino acids,

(c) a nucleotide sequence coding for the amino acid sequence<sup>(SEQ FD NO. 26)</sup>

C A (X'''<sub>1</sub> ... X'''<sub>n</sub>) D T Q Y F (IV)

in which X'''<sub>1</sub> ... X'''<sub>n</sub> represents a sequence of 5-7 amino acids,

(d) a nucleotide sequence which codes for an amino acid sequence that is at least 80 % identical with an amino acid sequence from (a), (b) or/and (c), or

(e) a nucleotide sequence which codes for an amino acid sequence with an equivalent recognition specificity for the peptide component of the T cell receptor ligand.

12. Nucleic acid as claimed in claim 11,  
wherein

the amino acid sequence X'<sub>1</sub> ... X'<sub>n</sub> is selected from the group comprising SSETNS, SSETSS, TS GTAS, RSGTGS, SSGTDS, SSGTRS, SSGSDS, SSSTGS, SSSTVS, SSSTLS, SSSTLF, SSSTAS, SSHTDS, SSDTLS, and SRWDSE<sup>(SEQ FD NO. 27)(SEQ FD NO. 28)(SEQ FD NO. 29)(SEQ FD NO. 30)(SEQ FD NO. 31)(SEQ FD NO. 32)(SEQ FD NO. 33)(SEQ FD NO. 34)(SEQ FD NO. 35)(SEQ FD NO. 36)(SEQ FD NO. 37)(SEQ FD NO. 38)(SEQ FD NO. 39)(SEQ FD NO. 40)(SEQ FD NO. 41)</sup>

13. Nucleic acid as claimed in claim 12,  
wherein

the amino acid sequence X'<sub>1</sub> ... X'<sub>n</sub> represents SSETNS, SSGTDS, TS GTAS, or RSGTGS<sup>(SEQ FD NO. 27)(SEQ FD NO. 28)(SEQ FD NO. 29)</sup>

14. Nucleic acid as claimed in claim 11,  
wherein  
the amino acid sequence X''<sub>1</sub> ... X''<sub>n</sub> represents  
<sup>(SEQ ID No: 12)</sup> <sup>(SEQ ID No: 43)</sup> SSGTSS<sub>1</sub> or SSDQGM<sub>1</sub> or the amino acid sequence  
<sup>SEV TO NA<sup>44</sup>)</sup> X'''<sub>1</sub> ... X'''<sub>n</sub> represents SADSFK<sub>1</sub>

15. Vector,  
wherein  
it contains at least one copy of a nucleic acid as  
claimed in one of the claims 10 to 14.

16. Cell,  
wherein  
it expresses a nucleic acid as claimed in one of  
the claims 10 to 14.

17. Cell,  
wherein  
it is transformed with a nucleic acid as claimed in  
one of the claims 10 to 14 or with a vector as  
claimed in claim 15.

18. Polypeptide,  
wherein  
it codes for a nucleic acid as claimed in one of  
the claims 10 to 14.

19. Polypeptide as claimed in claim 18,  
wherein  
it comprises the variable domain of the  $\beta$  chain of  
a human T cell receptor.

*II*

20. Polypeptide,  
wherein  
it has T cell receptor properties and is composed  
of a polypeptide as claimed in claim 8 or 9 as well  
as a polypeptide as claimed in claim 18 or 19 as  
subunits.

*Antibody  
Claims*

21. Polypeptide as claimed in one of the claims 8, 9,  
18, 19 or 20,  
wherein  
it is coupled to a labelling group or a toxin.

22. Polypeptide as claimed in one of the claims 8, 9,  
18, 19, 20 or 21,  
wherein  
it is present in an oligomerized form.

*IV*

23. Antibody against a polypeptide as claimed in one of  
the claims 8, 9, 18, 19, 20, 21 or 22 which is  
directed against a region which is responsible for  
recognizing the peptide ligand.

24. Antibody as claimed in claim 23,  
wherein  
it is directed towards a CDR3 region.

*A*

25. T cell,  
wherein  
it contains a T cell receptor as claimed in claim  
20.

I  
II  
III  
~~IV~~ 23  
V

26. Pharmaceutical composition which contains as active component a nucleic acid as claimed in one of the claims 1 to 4 or 10 to 14, a polypeptide as claimed in one of the claims 8, 9 or 18 to 23, a peptide ligand against the polypeptide, an antibody as claimed in claim 23 or 24 or a cell as claimed in claim 6, 7, 16, 17 or 25 optionally together with other active components as well as common pharmaceutical auxiliary agents, additives or carrier substances.

VI

27. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for the diagnosis of tumour diseases or a predisposition for a tumour disease.

28. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for monitoring the course of the disease in a tumour disease.

VII

29. Use as claimed in claim 27 or 28, where in the detection of T cells that express a polypeptide as claimed in claim 20 as the T cell receptor is carried out in a sample liquid by a nucleic acid hybridization assay, an immunoassay, a test for the binding of specific peptide ligands or a specific T cell activity test.

unbroken  
MDC

VIII

30. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for the prevention or therapy of a tumour disease.

*XII* 31. Use as claimed in claim 30,  
wherein  
the agent is suitable for the stimulation of the  
growth of T cells that express a polypeptide as  
claimed in claim 20 as a T cell receptor.

32. Use as claimed in claim 31,  
wherein  
the agent is suitable for growth stimulation of the  
T cells in vivo.

33. Use as claimed in claim 31 or 32,  
wherein  
the agent for growth stimulation comprises the  
peptide ligand of the T cell receptor or/and the  
entire molecule from which the peptide ligand is  
derived or a fragment thereof.

34. Use as claimed in claim 31 or 32,  
wherein  
the growth stimulation includes an antibody that  
specifically activates the T cell receptor.

35. Use as claimed in claim 31,  
wherein  
the growth stimulation is carried out by isolating  
specific T cells, in vitro expansion and subsequent  
administration of expanded T cells.

36. Use as claimed in one of the claims 27 to 35,  
wherein  
the tumour disease is a kidney cell carcinoma.

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*unpublished MDC*

37. Process for the isolation of T cells that express a polypeptide as claimed in claim 20 as a T cell receptor,  
wherein  
a sample containing T cells is contacted with an agent that binds specifically to the CDR3 region of the T cell receptor. T cells that react with the agent are identified and optionally separated from other T cells.

38. Process as claimed in claim 37,  
wherein  
the agent is selected from the peptide ligand of T cells, a MHC peptide complex containing the peptide ligand or/and an anti-TCR antibody.

39. Process as claimed in claim 37 or 38 additionally comprising an in vitro expansion of T cells.

40. Process for the isolation of T cells which express a polypeptide as claimed in claim 20 as the T cell receptor,  
wherein  
nucleic acid sequences that code for the T cell receptor are introduced into a T cell line and are made to express therein.

41. Process for the isolation of T cells that express a polypeptide as claimed in claim 20 as the T cell receptor,  
wherein  
nucleic acid sequences which code for the T cell

receptor are introduced into the germ line of an animal and the T cells are isolated from the resulting transgenic animal or descendants thereof.

42. Transgenic animal,  
wherein  
it expresses a polypeptide as claimed in claim 20  
as the T cell receptor.

43. Method for the identification of peptide ligands of a T cell receptor as claimed in claim 20 comprising the steps:

- (a) isolating RNA from tumour tissue,
- (b) converting the RNA into double-stranded cDNA molecules,
- (c) introducing the cDNA molecules into host cells to obtain a cDNA bank,
- (d) transfecting eukaryotic recipient cells with aliquots of the cDNA bank wherein (i) cotransfection with HLA-A\*0201 DNA is carried out or (ii) HLA-A\*0201 positive recipient cells are used,
- (e) testing the transfected recipient cells for their ability to stimulate T cells,
- (f) identifying a cDNA sequence which codes for the antigen which contains the peptide ligand and

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(g) identifying the sequence of the peptide ligand.

44. Method as claimed in claim 43,  
wherein  
step (e) comprises testing for the ability to lyse  
TNF-sensitive cells.

Add 4

Add G1

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